

# Successful treatment of resistant giant cell arteritis with etanercept

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Giant cell arteritis (GCA) is a systemic medium to large cell vasculitis that predominantly affects the elderly population.<sup>1</sup> Initial high dose corticosteroids are the cornerstone of treatment, which is subsequently tapered.<sup>2</sup> However, disease flares are not uncommon and corticosteroid related side effects are frequent.<sup>3</sup>

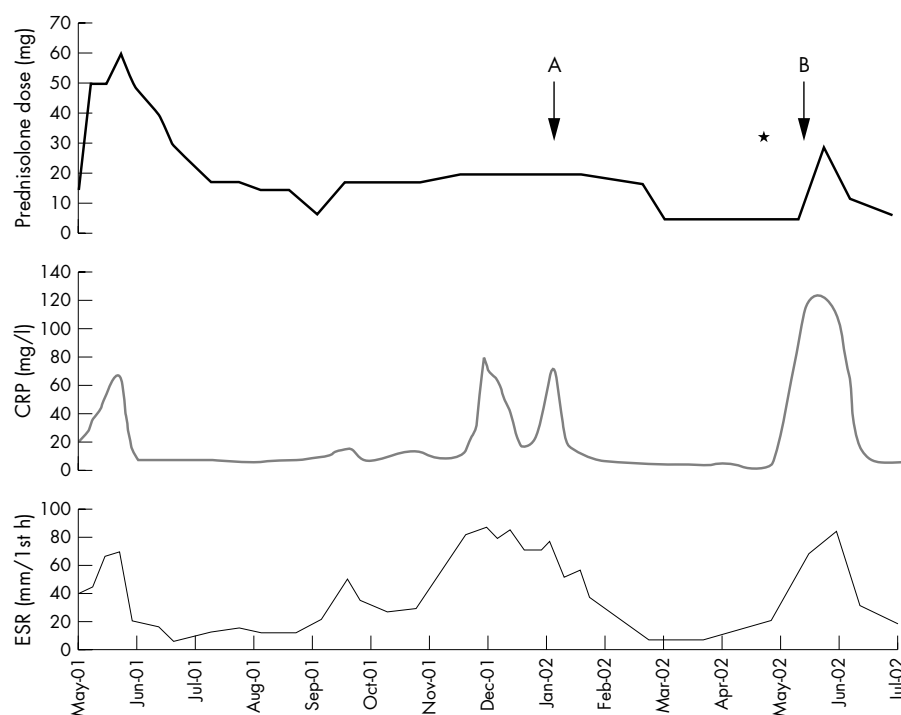
The limitations of corticosteroids in the treatment of some cases of GCA have led to the evaluation of other strategies using steroid sparing agents.<sup>4–7</sup> In two previous studies patients with resistant GCA were treated with infliximab, a monoclonal chimeric antibody directed against tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) that binds circulating and membrane bound TNF, with promising results.<sup>6,7</sup> The rationale for this approach was that the vasculitic lesions in GCA had prominent macrophage infiltration where excess TNF $\alpha$  production had been demonstrated by immunohistochemistry.<sup>8</sup>

We report the case of a patient who was treated with the anti-TNF $\alpha$  agent etanercept, which is the fusion protein of the extracellular ligand binding portion of the p75 TNF receptor and the Fc portion of IgG1, on the basis that the GCA could not be controlled and that complications of high dose corticosteroid treatment appeared imminent.

## CASE REPORT

The patient was an 80 year old man whose initial symptoms in March 2001 were diffuse aching of the shoulders, arms, and legs, profound morning stiffness with no headaches but a high C reactive protein (CRP) of 77 mg/l. Treatment was started with prednisolone 15 mg daily with a moderate clinical improvement in the following months, but his inflammatory markers remained high. He subsequently developed headaches and was referred to the rheumatology department in May 2001. He had temporal tenderness in addition to his original symptoms; a temporal artery biopsy was therefore performed. The biopsy failed to confirm arteritis and a diagnosis of GCA was hence made based on the clinical findings. His steroids were increased to 60 mg daily with improvement of his headaches and inflammatory markers (erythrocyte sedimentation rate (ESR) 21 mm/1st h, CRP 12 mg/l) (fig 1). Treatment was also started with prophylactic alendronate 70 mg weekly together with calcium and vitamin D. Over the following six months his prednisolone could not be tapered below 20 mg daily.

In November 2001 he had a transient ischaemic attack with sudden onset weakness in the left arm which occurred when his ESR was 84 mm/1st h. His blood pressure, pulse, lipids, and



**Figure 1** The effect of etanercept on C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of the patient. Etanercept treatment was started at point A, when symptoms were uncontrolled with prednisolone 20 mg daily, at a stage when the patient had visual symptoms. The patient improved and was able to reduce the dose of the steroid. He discontinued the etanercept in May 2002 and consequently his disease flared (shown by the asterisk). The recurrence of his initial GCA symptoms coupled with an increase of his inflammatory markers prompted us to restart the etanercept treatment (point B). He responded well, the inflammatory markers fell and the dose of prednisolone was quickly tapered to 7.5 mg/day.

electrocardiograph were normal, and this episode was attributed to the arteritis. An insufficiency fracture was also suspected when he developed severe rib pain after coughing. He had a pre-existing history of macular degeneration and glaucoma and had complained of gradual visual deterioration during high dose corticosteroid treatment. No change in visual acuity was demonstrated and his intraocular pressures were normal. His blood glucose was also normal.

In view of the persistently high dose of steroids used, the failure to suppress the inflammation, the complications, and the concern about the steroids contributing to normal pressure glaucoma, the patient was offered etanercept in February 2002. Treatment was started with 25 mg subcutaneously twice weekly and he continued to receive prednisolone 20 mg daily. Within the following month there was a dramatic resolution of the myalgia and stiffness around his shoulders, arms, neck, and thighs. His corticosteroid dose was tapered to 5 mg daily and the frequency of etanercept was decreased to once every eight days.

The patient, thinking that he was cured, stopped taking the etanercept. Two weeks after he stopped he contacted the rheumatology department with a severe flare of his disease (ESR 71 mm/1st h, CRP 123 mg/l) and return of the symptoms he had before the initial treatment with etanercept. Treatment was therefore restarted with etanercept without adjusting his steroid dose initially. No immediate response was evident so the prednisolone was increased to 30 mg daily two weeks later, and his symptoms resolved within one month with associated normalisation of his ESR and CRP. Six months after starting etanercept he is maintained on a dose of 25 mg every four days and prednisolone 5 mg and 7.5 mg on alternate days.

## DISCUSSION

TNF $\alpha$  is a proinflammatory cytokine with a pivotal role in the pathogenesis of GCA.<sup>8,9</sup> As far as we know, this is the first report suggesting that etanercept may have a role in the treatment of resistant GCA. This single case does not allow us to draw definitive conclusions from our observation. Nevertheless, the dramatic responses following treatment, the flare of disease on discontinuation, and the successful re-induction of remission suggest that etanercept might be

useful in resistant GCA. We noted that remission induction was delayed and that relatively high dose corticosteroids had to be given when etanercept was started, but that this could be quickly tapered in the following weeks. The advantage of etanercept as a steroid sparing agent in GCA is the ease of administration and the ability to taper the dose depending on clinical and laboratory responses. Further studies are warranted to determine the efficacy of etanercept in resistant GCA.

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# Bilateral subdural effusion in a patient with neuro-Behçet's disease

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**T**he central nervous system is sometimes affected in patients with Behçet's disease.<sup>1</sup> Meningoencephalitis and brainstem lesions are the most common problems. The appearance of subdural effusion has been rarely reported. Our patient, who had neuro-Behçet's disease with massive bilateral subdural effusion, was successfully treated with steroid pulse therapy.

## CASE REPORT

The patient (a 45 year old man) first developed polyarthralgia, fever, recurrent oral aphthosis, and headache in 1986. In 1987 he had a genital ulcer and positive pathergy test. Thus, he ful-

filled the international criteria for the diagnosis of Behçet's disease. He had two cycles of steroid pulse therapy, and his symptoms including headache subsided. In 1995 an episodic exacerbation of the neuro-Behçet's disease occurred, accompanying parkinsonism and abnormal cerebral spinal fluid (CSF) findings (cell 5/3, protein 0.97 g/l, IgG 0.07 g/l). The symptoms improved after treatment with prednisolone 40 mg/day + colchicine 1 mg/day.

In December 2000 he began to have severe oral aphthosis and folliculitis, even though he had been taking low doses of steroids + colchicine. On 4 January 2001 he was admitted to our hospital because of fever (38–39°C), steppage gait,